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EDITORIAL COMMENT

At Arm's Length

Radiation Safety During Radial Percutaneous Coronary Intervention*

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The transradial approach (TRA) to coronary angiography and percutaneous coronary intervention (PCI) is becoming increasingly popular in the United States and internationally (1,2). In appropriately selected patients, registry and randomized trial data have indicated its superiority for reduced mortality, less frequent access site bleeding complications, and possibly earlier hospital discharge (3-5). The benefit appears to be greatest among operators and sites with high PCI volume and high TRA usage, as well as in patients with ST-segment elevation myocardial infarction (STEMI) (6,7). The primary obstacles to TRA adoption have consisted of the new skillset required of previous transfemoral operators and concern over increased radiation exposure during the procedure. The former concern is prevalent among high-volume operators; the latter among low-volume operators (8). The literature concerning radiation exposure has been varied, indicating a substantial increase in operator (and patient) exposure, a minimal difference, or no difference. In the current issue of the *Journal*, the MATRIX (Minimizing Adverse Haemorrhagic Events by Transradial Access Site and Systemic Implementation of AngioX) trial investigators lend the prestige (and sample size) of their study to address whether, in fact, TRA increases operator and patient radiation exposure (9).

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The design and overall results of MATRIX are well known. A total of 8,404 patients with acute coronary syndromes were randomized to undergo angiography and PCI using either TRA or a transfemoral approach (TFA). Ultimately, the study found that mortality was reduced from 2.2% to 1.6% ($p = 0.045$) with TRA versus TFA angiography plus PCI, and major bleeding was reduced as well (2.3% vs. 1.6%; $p = 0.0092$) (3). These findings added to the evidence that PCI operators should familiarize themselves with the skills required for TRA, even if their preferred access is transfemoral, or ought to assure that a skilled radial operator is available when a patient is judged to require TRA.

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The RAD-MATRIX (Radiation-MATRIX) sub-study, reported by Sciahbasi et al. (9) in this issue of the *Journal*, was designed to dispel the notion that radiation exposure is increased when transradial PCI is performed by experienced operators. Among 7,570 procedures in the trial, patient radiation exposure, reported as dose-area product measured at the gantry collimator, was slightly higher for TRA (65 $Gy \cdot cm^2$ vs. 59 $Gy \cdot cm^2$; $p = 0.0001$). Detailed information is available for operator exposure in a smaller subset ($n = 777$) of cases. Operators wore dedicated dosimeters at forehead level, left wrist, and outside the chest pocket of lead aprons. The study's primary endpoint was operator exposure at the level of the thorax. Presumably this site was chosen because the sternum, spine, and pelvis are the primary sites containing marrow-forming elements in adults and are expected to be the most susceptible to radiation-induced mutagenesis. The study was designed to show noninferiority of TRA with a margin of 25 μSv. Trends toward increased exposure at the head and wrist were not statistically significant. However, the dose received at chest level was 88% higher (77 μSv; interquartile range [IQR]: 40 to 112 μSv, vs. 41 μSv; IQR: 23 to 59 μSv; $p = 0.02$). The 36-μSv difference fell outside the noninferiority margin, so transradial PCI was, in fact, inferior to femoral PCI. In a smaller number of comparisons performed for left versus right TRA, no differences were observed. It is also worth noting that given the geometric relationship(s) between placement of the chest and head badges, the surprising absence of significant differences in putative eye dose raises questions about the customary use of thyroid collar readings to estimate the eye dose.

These findings should be both encouraging and alarming. They resonate particularly loudly because they represent the outcomes of an expert group of operators. A previous report from the RIVAL (Radial vs Femoral Access for Coronary Intervention) investigators offered findings that are basically concordant with those from MATRIX. The 3% relative difference in dose-area product between TRA and TFA (52.8 $Gy \cdot cm^2$ vs. 51.2 $Gy \cdot cm^2$, respectively) was not statistically different. However, the smaller sample size and the smaller proportion of PCI (62.4% in RIVAL vs. 80.1% in MATRIX) resulting in shorter fluoroscopy times may limit the ability of RIVAL to detect a difference (10). Notably though, when the analysis was stratified according to operator and center volume, cases performed by operators within the lowest tertile (defined as <60 radial PCI/year) had higher air kerma and dose-area product for TRA versus TFA (10).

In contrast, participation in MATRIX required an operator to have completed >75 radial interventions in the year before the trial (3), a value well above the inflection point at which the TRA learning curve has been observed to flatten. By comparison, in the 2009-2012 harvest of National Cardiovascular Database Registry data, only 6% of operators had performed >100 transradial PCIs in a 3-year period (11). Currently, the complexity of coronary interventional cases is increasing as the number of chronic total occlusion PCIs increases and interest in complex higher-risk indicated patient PCI grows. Given the acute nature of the patient presentation in MATRIX (nearly 50% were STEMI), one wonders whether the specific procedures were technically more straightforward than the average case (fluoroscopy time was 10.2 min for radial and 9.1 min for femoral cases; $p < 0.0001$), leading to an underestimation of the higher day-to-day radiation exposure for TRA operators.

Radiation mutation and mutagenesis are stochastic phenomena. There is a mathematical probability of damage at any dose, albeit at very low exposures the risk is very low. As the RAD-MATRIX investigators indicated, the small differences in patient radiation exposure predict negligible increases in cancer risk that are mitigated by the shortened expected survival among patients who present with acute coronary syndrome. Furthermore, any small radiation risk to the patient was easily outweighed by the mortality benefit present in MATRIX. Unfortunately, this may not be true for the PCI operators.

Paradoxically, patients selected for radial PCI are usually younger and, at the time the procedure is begun, and are usually anticipated to require less complex procedures (12). In other words, they are less likely to die of cardiac disease and thus have increased lifetime risk for radiation-induced malignancies. Although parallel data concerning PCI operators are not published, it is likely that those who choose the radial approach are also younger and are themselves at greater risk for the adverse consequences of radiation exposure. The problem is that although radiation exposure is generally acknowledged as an occupational hazard of interventional cardiology, it is rarely taken seriously. It is common to see individuals performing procedures without wearing leaded eyewear, or casually strolling into catheterization labs without wearing appropriate aprons. The topic is often approached jocularly with comments about childbearing with little thought given to cancer risk. However, the radiation-induced health risk to adults is nontrivial and outweighs by an order of magnitude any risk for hereditary damage (13).

While the toxicity of radiation has been appreciated since the time of the Curies, the dataset concerning clinical events in medical personnel has remained anecdotal. Perhaps the clearest evidence of tissue damage comes from the world of ophthalmology, probably because the lens of the eye is one of the most radiosensitive tissues in the body (14) and because such changes are easy to observe. Ocular exposure guidelines, therefore, are based on risk for radiation cataract, the primary pathology noted after ocular exposure to ionizing radiation. Until very recently, ocular exposure guidelines were based on the assumption that radiation cataract is a deterministic event requiring threshold doses >2 Gy. Newer findings, however, in populations exposed to far lower doses of radiation, including those involved in interventional medical procedures, indicated dose-related lens opacification might occur at significantly lower doses.

These observations led the International Commission on Radiological Protection (ICRP) to issue new

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recommendations that lower the putative threshold values for radiation cataract to 0.5 Gy from previous values of 2 to 8 Gy, regardless of whether the exposure was acute, prolonged, or chronic (15). At the same time, recommended occupational lens exposure limits were lowered from 150 mSv/year to 20 mSv/year averaged over 5 years, with no single year exceeding 50 mSv.

This recommendation has had an immediate impact on the Directive of the European Commission and the International Basic Safety Standards issued by the International Atomic Energy Agency (IAEA) (16). In response to a request by the U.S. Nuclear Regulatory Commission for comment on proposed rulemaking for potential changes to 10 CFR Part 20, Standards for Protection Against Radiation, the Health Physics Society noted significant concern about the effect of radiation-induced ocular damage on the performance of health care workers "…prior to a documented clinical need for cataract surgery, there may be accompanying progressive decreases in visual acuity, contrast sensitivity and visual function that may negatively impact worker performance" (17,18). Nevertheless, in 2016, the National Council on Radiation Protection and Measurements (NCRP) re-evaluated the clinical and experimental evidence for the risk of radiation-induced cataract, as well as the new ICRP and IAEA recommendations in light of their practical and cost implications, and concluded that, at the present time, no changes were warranted in U.S. regulations (19). The committee did note, however, "There is an urgent need for NCRP to develop a comprehensive evaluation of the overall effects of radiation on the lens of the eye… Such a comprehensive evaluation should include a further reassessment of the lens of the eye dose limit values" (20). With respect to specific findings among interventional medical workers, a recent study of interventional cardiologists and catheterization laboratory nurses, who all underwent detailed ophthalmic examinations, Vano et al. (21) found that 50% of interventional cardiologists and 41% of nurses had lens pathology consistent with and characteristic of radiation exposure, compared with 10% among a control group. Similar findings have been reported by other groups (22).

Although the data concerning lens opacities and radiation associated lens changes among interventional cardiology staff are compelling, facts concerning cancer risk in such individuals are suggestive but still controversial. Cardoso et al. (23) studied the deoxyribonucleic acid of lymphocytes in 16 health care workers, 8 of whom were exposed to chronic low-level radiation and 8 of whom served as controls. Chromosomal aberrations and sister chromatid exchanges, both indexes of mutation, were higher among subjects exposed to radiation. Interestingly, the level of radiation exposure did not predict the frequency of chromosomal abnormalities, a finding that highlights the stochastic nature of the risk. The estimated absorbed doses in some of the subjects with evidence of mutations were the equivalent of only 200 times the median and 85 times the 75th percentile of thorax exposure among operators performing radial PCI in MATRIX (23). These observations imply that after only 200 cases, or fewer than 100 complex cases (which might be performed in only 1 or 2 years), a busy TRA operator would be likely to develop lymphopoietic mutations.

Although the findings of MATRIX are unlikely to impede the swelling tide of TRA, the implications are very important. Obviously, they should prompt radial and femoral operators to heed radiation safety principles, none of which are terribly complex. They also point to a serious knowledge gap. Put simply, the measures collected thus far have been surrogates for clinical events. Actual outcome data have been anecdotal and would never meet the rigorous standards that we normally require to assess medical diagnostic tests or therapies. Just as the approach to clinical problems has evolved over the last several decades from therapies based on case series to rigorous controlled clinical trials and sophisticated analyses of rigorously collected registry data, we need comparable data concerning the safety of PCI for operators and staff.

There has been movement in this direction, including the founding of the Organization for Occupational Safety in Interventional Fluoroscopy, and position statements from various professional societies. However, systematic recording of clinical outcomes among health care workers exposed to radiation simply does not exist. Collecting these data is not particularly appealing since most of the operators are younger than the investigators and are therefore likely to outlive them. Not only would such studies be exceptionally useful, they would help motivate appropriate attention to radiation safety and perhaps accelerate the development of radiation-sparing technology.

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REFERENCES

1. Adamo M, Byrne RA, Baumbach A, Haude M, Windecker S, Valgimigli M. Assessing the cardiology community position on transradial intervention and the use of bivalirudin in patients with acute coronary syndrome undergoing invasive management: results of an EAPCI survey. EuroIntervention 2016;12:1154–63.

2. Feldman DN, Swaminathan RV, Kaltenbach LA, et al. Adoption of radial access and comparison of outcomes to femoral access in percutaneous coronary intervention: an updated report from the national cardiovascular data registry (2007-2012). Circulation 2013;127:2295–306.

3. Valgimigli M, Gagnor A, Calabro P, et al. Radial versus femoral access in patients with acute coronary syndromes undergoing invasive management: a randomised multicentre trial. Lancet 2015;386:2394.

4. Kwok CS, Khan MA, Rao SV, et al. Access and non-access site bleeding after percutaneous coronary intervention and risk of subsequent mortality and major adverse cardiovascular events: systematic review and meta-analysis. Circ Cardiovasc Interv 2015;8:e001645.

5. Amin AP, Patterson M, House JA, et al. Costs associated with access site and same-day discharge among medicare beneficiaries undergoing percutaneous coronary intervention: an evaluation of the current percutaneous coronary intervention care pathways in the United States. J Am Coll Cardiol 2017;10:342–51.

6. Gutierrez A, Tsai TT, Stanislawski MA, et al. Adoption of transradial percutaneous coronary intervention and outcomes according to center radial volume in the Veterans Affairs Healthcare System. Insights from the Veterans Affairs Clinical Assessment, Reporting, and Tracking (CART) program. Circ Cardiovasc Interv 2013;6:336–46.

7. Mehta SR, Jolly SS, Cairns J, et al. Effects of radial versus femoral artery access in patients with acute coronary syndromes with or without ST-segment elevation. J Am Coll Cardiol 2012;60:2490–9.

8. Helfrich CD, Tsai TT, Rao SV, et al. Perceptions of advantages and barriers to radial-access percutaneous coronary intervention in VA cardiac catheterization laboratories. Cardiovasc Revasc Med 2014;15:329–33.

9. Sciahbasi A, Frigoli E, Sarandrea A, et al. Radiation exposure and vascular access in acute coronary syndromes: the RAD-MATRIX trial. J Am Coll Cardiol 2017;69:2530–7.

10. Jolly SS, Cairns J, Niemela K, et al. Effect of radial versus femoral access on radiation dose and the importance of procedural volume: a substudy of the multicenter randomized RIVAL trial. J Am Coll Cardiol Intv 2013;6:258–66.

11. Hess CN, Peterson ED, Neely ML, et al. The learning curve for transradial percutaneous coronary intervention among operators in the United States: a study from the National Cardiovascular Data Registry. Circulation 2014;129:2277–86.

12. Hamon MCP, van't Hof A, Ten Berg J, et al. Impact of arterial access site on outcomes after primary percutaneous coronary intervention: a pre-specified subgroup analysis from the EUROMAX trial. Circ Cardiovasc Interv 2015;8:e002049.

13. Hall EG, Giaccia AJ. Radiobiology for the Radiologist. 7th Ed. Philadelphia, Pennsylvania: Lippincott WIlliams & Wilkins, 2012.

14. Kleiman NJ. Radiation cataract. Ann ICRP 2012;41:80–97.

15. Stewart FA, Akleyev AV, Hauer-Jensen M, et al. ICRP publication 118: ICRP statement on tissue reactions and early and late effects of radiation in normal tissues and organs—threshold doses for tissue reactions in a radiation protection context. Ann ICRP 2012;41:1–322.

16. Behrens R. Monitoring the eye lens: how do the international organisations react? Radiat Prot Dosimetry 2015;164:75–8.

17. Health Physics Society. Comments in Response to Advance Notice of Proposed Rulemaking for Potential Changes to 10 CFR Part 20, Standards for Protection Against Radiation (letter). Available at: http://hps.org/documents/hps_nrc_response_to_anpr_10cfr20_15-05-20.pdf. Accessed on March 16, 2017.

18. Lundström M, Goh PP, Henry Y, et al. The changing pattern of cataract surgery indications: a 5-year study of 2 cataract surgery databases. Ophthalmology 2015;122:31–8.

19. National Council on Radiation Protection and Measurement. NCRP Draft SC 1-23 Commentary: Guidance on Radiation Dose Limits for the Lens of the Eye. Available at: http://www.aapm.org/pubs/enews/documents/LensoftheEyeNCRPM1603.pdf. Accessed on March 16, 2017.

20. Dauer LT, Ainsbury EA, Dynlacht J, et al. Status of NCRP Scientific Committee 1-23 Commentary on Guidance on Radiation Dose Limits for the Lens of the Eye. Health Phys 2016;110:182–4.

21. Vano E, Kleiman NJ, Duran A, Romano-Miller M, Rehani MM. Radiation-associated lens opacities in catheterization personnel: results of a survey and direct assessments. J Vasc Interv Radiol 2013;24:197–204.

22. Jacob S, Boveda S, Bar O, et al. Interventional cardiologists and risk of radiation-induced cataract: results of a French multicenter observational study. Int J Cardiol 2013;167:1843–7.

23. Cardoso RS, Takahashi-Hyodo S, Peitl P Jr., Ghilardi-Neto T, Sakamoto-Hojo ET. Evaluation of chromosomal aberrations, micronuclei, and sister chromatid exchanges in hospital workers chronically exposed to ionizing radiation. Teratog Carcinog Mutagen 2001;21:431–9.

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